OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2022;7(2):232-238 *Online Türk Sağlık Bilimleri Dergisi 2022;7(2):232-238*

Radyoaktif İyot Tedavisi Uygulanan Hipertiroidili Hastalarda Kemik Mineral Yoğunluğunun DEXA ile Değerlendirilmesi

Evaluation of Bone Mineral Density with DEXA in Hyperthyroid Patients Treated with Radioactive Iodine Treatment

[1]Huri Tilla ILCE

[1]Sakarya University Faculty of Medicine Department of Nuclear Medicine, Sakarya Turkey

Huri Tilla Ilce: https://orcid.org/0000-0002-8672-707X

ÖZ

Amaç: Bu çalışmada hipertiroidili hastalarda kemik mineral yoğunluğu (KMY) ve radyoaktifiyot (RAI) tedavisinin araştırılması ve RAI tedavisinin KMY üzerine etkilerinin değerlendirilmesi amaçlanmıştır. Sonuçlar güncel literatürle gözden geçirildi.

Materyal ve Metot: Hipertiroidi nedeniyle RAİ uygulanan hastaların tedavi öncesi ve sonrası, tiroid sintigrafileri, tiroid fonksiyonları ve kemik dansitometresi sonuçları değerlendirildi.

Bulgular: Yaş ortalaması 58,4±11,1 olan 46 hasta (31 kadın, 15 erkek) incelendi. Hastaların 3'ü (%7) Graves' hastalığı (GH), 24'ü (%52) toksik adenom (TA), 19'u (% 41) toksik multi nodüler guatr (TMNG) idi. RAİ öncesi ortalama değerler; TSH 0,005 IU/mL, sT3 12,33 pmol/L, sT4 17,38 pmol/L, vertebra T skoru (-)1,15, Z skoru 0,33, KMY 0,99g/cm^2, femur T Skoru (-)1,30, Z Skoru 0, KMY 0,83g/cm^2 idi. RAİ tedavisinden bir yıl sonra ortalama değerler; TSH 1,19 IU/mL, sT3 3,44 pmol/L, sT4 11,33 pmol/mL, vertebra T skoru (-) 0,85, Z skoru 0,04, KMY 1,03g/cm^2, femur T Skoru (-)1,0, Z Skoru 0,30, KMY 0,87 g/cm^2 idi.

Sonuç: Seçilmiş hipertiroidili hastalarda RAİ başarı ile uygulanabilir. Hipertiroidi sırasında oluşan KMY'deki azalma RAİ sonrası düzelmektedir. Sonuçlar güncel literatürle uyumludur.

Anahtar Kelimeler: Hipertiroidi, kemik mineral yoğunluğu, radyoaktif iyot

ABSTRACT

Objective: This study aimed to investigate bone mineral density (BMD) and radioactive iodine (RAI) treatment in patients with hyperthyroidism and to evaluate the effects of RAI treatment on BMD. The results were reviewed with current literature.

Materials and Methods: Thyroid scintigraphy, thyroid functions, DEXA results of patients were evaluated before and after RAI.

Results: Forty-six patients (31 female, 15 male) with a mean age of 58.4±11.1 were studied. Three (7%) patients had Graves' disease (GH), 24 (52%) toxic adenomas (TA), 19 (41%) toxic multinodular goiters (TMNG). Mean values before RAI; TSH 0.005 IU/mL, fT3 12.33 pmol/L, fT4 17.38 pmol/L, vertebral T score (-)1.15, Z score 0.33, BMD 0.99g/cm^2, femur T-Score (-)1.30, Z-Score 0, BMD 0.83 was g/cm^2. Mean values after RAI; TSH 1.19 IU/mL, fT3 3.44 pmol/L, fT4 11.33 pmol/mL, vertebral T score (-) 0.85, Z score 0.04, BMD 1.03g/cm^2, femur T-Score (-) 1.0, Z-Score 0.30, BMD 0.87 was g/cm^2.

Conclusion: RAI can be successfully used in selected patients with hyperthyroidism. The decrease in BMD improves after RAI. The results are consistent with current literature.

Keywords: Bone mineral density, hyperthyroidism, radioactive iodine

Sorumlu Yazar / Corresponding Author:
Huri Tilla Ilce
Sakarya University School of Medicine Department of Nuclear Medicine Sakarya Turkey
Tel: +905336214910
E-mail: hilce@sakarya.edu.tr

Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 22/02/2022
Kabul Tarihi/ Accepted: 16/03/2022
Online Yayın Tarihi/ Published: 01/06/2022

Atıf / Cited: İlce HT. Radyoaktif İyot Tedavisi Uygulanan Hipertiroidili Hastalarda Kemik Mineral Yoğunluğunun Dexa ile Değerlendirilmesi. *Online Türk Sağlık Bilimleri Dergisi* 2022;7(2):232-238. doi: 10.26453/otjhs.1077111

INTRODUCTION

The primary causes of hyperthyroidism in adults are Graves' disease (GD), toxic adenoma (TA), and toxic multinodular goiter (TMNG). Hyperthyroidism is characterized by increased levels of free triiodothyronine (fT_3), free thyroxine (fT_4), and suppression of thyroid-stimulating hormone (TSH). The term thyrotoxicosis is a clinical syndrome characterized by an increase in the level of fT_3, fT_4, and/or both, and the acceleration of body metabolism because of suppression of TSH. While most patients with thyrotoxicosis have hyperthyroidism, in some patients' thyrotoxicosis depends on thyroiditis and intake of exogenous thyroid hormones.[1]

The primary treatment options for hyperthyroidism are antithyroid drugs, radioactive iodine (RAI) therapy, and surgery. The use of treatment options varies according to thyroid centers. Although antithyroid drugs are generally selected as the initial treatment, the permanent cure rate is low, and the recurrence rate is high when the treatment is stopped. Furthermore, there are side effects of drugs, and problems encountered with patient compliance with regular medication intake.[2] Surgery is another option. The rate of complete treatment is high but serious complications such as recurrent laryngeal nerve injury, hypoparathyroidism, and temporary or permanent hoarseness may be encountered. Considering these negative consequences, RAI has been increasingly used to treat hyperthyroidism for many years because it has fewer complications. RAI improves hyperthyroidism by causing diffuse radiation thyroiditis in the gland-associated chronic inflammatory response, fibrosis, and atrophy. Mostly, it performs this with a single dose of treatment.[3,4]

Physiological levels of thyroid hormones are essential for the healthy development of bone. Hyperthyroidism accelerates bone turnover and increases cortical bone porosity; it reduces cortical and trabecular bone mass and is more pronounced in cortical bone.[5]

There are not enough studies about the effects of RAI treatment on bone metabolism in hyperthyroid patients. Nevertheless, in our study, patients who received RAI treatment because of GD, TA, and TMNG were evaluated. It was aimed to evaluate the effects of improvement on bone metabolism with BMD measurements while hyperthyroidism was improving with RAI treatment and the results were reviewed with the current literature.

MATERIALS AND METHODS

Ethics Committee Approval: This study was designed by the Declaration of Helsinki Principles and approved by Sakarya University Faculty of Medicine Ethics Committee (Date: 03.01.2022, decision no: 560).

Forty-six patients who received RAI therapy for hyperthyroidism between 2007-2008 were included in this study. The hyperthyroidism diagnosis was made by clinical investigation, ultrasonography, thyroid function tests, and scintigraphy.

Basal TSH, fT_3, fT_4, and bone mineral densities of patients were measured before receiving RAI treatment.

Thyroid function tests were evaluated using the electrochemiluminescence immunoassay (ECLIA) method with Roche E170 device (Roche diagnostic immunoassay analyzers, Manheim, Germany). Accordingly, reference intervals were fT_3: 3.1-6.8 pmol/L, fT_4: 12-20 pmol/L, TSH: 0.27–4.2 IU/mL.

BMD was evaluated by bone densitometry (DEXA). T-score of total vertebrae, Z-score of total vertebrae, BMD values of vertebrae, T-score of total femur, Z-score of total femur, BMD values of femur were measured by densitometry. Patients without osteoporosis were included in this study. We excluded patients with significant ophthalmopathy, thyroid malignancy, mental illness in this study.

The RAI treatment was administered in fixed doses. Treatment doses were 15 mCi for GD, 20 mCi for TA, and 25 mCi for TMNG. Fixed-dose application was preferred as there was no uptake device in our department.

The antithyroid drugs that the patients were taking were stopped ten days before the treatment. It was ensured that patients did not consume foods containing iodine. On the day of treatment, the patient was asked to fast to increase the RAI absorption. Before the application, the patient was informed by the physician about the necessary warnings, the success of the treatment, and possible complications. The routine rules that the patient should pay attention to before and after RAI treatment were explained and the precautions that the patient should follow after the treatment to protect from the side effects of RAI were explained.

TSH, fT_3, fT_4, and BMD levels of patients were measured in the first year after RAI treatment. Thyroid function tests were also performed at the third and sixth months to evaluate the patients' response to treatment.

Statistical Evaluation: Statistical evaluations were made using SPSS 24.0. Numerical data were evaluated by Kolmogorov–Smirnov, and Shapiro–Wilk tests to determine whether it fits the normal distribution. The difference before and after the RAI treatment was evaluated with the paired sample T-Test for normally distributed data, and the Wilcoxon signed ranks test for non-normally distributed data considering the symmetry assumption. Independent sample t-test or Mann–Whitney U test was used to compare numerical data between men and women

considering the distribution. Descriptive statistics of normally distributed data were given as mean±SD, and data with non-normal distribution were given as median, minimum and maximum values. The statistical significance was accepted as $p < 0.05$.

RESULTS

To detect alterations in BMD in patients who were received RAI, thyroid function tests and BMD measurements before and after treatment were performed in 46 patients with hyperthyroidism for 1 year. Note that 31 (67%) of the patients were female and 15 (33%) were male. The mean age of women was 58.2±12.2, the mean age of men was 58.8±8.8, and the mean age of all patients was 58.4±11.1. Three of the patients (7%) were GD, 24 (52%) were TA, and 19 (41%) were TMNG. When the thyroid function values, the total vertebrae, and femur BMD values of the patients before and after RAI treatment were compared, the results were found to be statistically significant. The results are summarized in Table 1.

It is observed that post-treatment levels of TSH increased, fT_3 and fT_4 decreased. There is an increase in BMD values except the vertebrae Z-score. The changes observed in thyroid functions and BMD levels were statistically significant ($p < 0.05$) (Table 1).

Table 2 shows the comparative thyroid function values of male and female patients before and after radioactive iodine treatment.

Table 3 shows comparative total vertebrae BMD values and the comparative total femur BMD values of female and male patients before RAI treatment.

Table 4 shows the comparative total vertebrae BMD values and the comparative total femur BMD values of female and male patients after RAI treatment.

Table 1. Thyroid function tests and bone mineral density average values before and after radioactive iodine treatment.

Parameters	Before RAI	After RAI	p-value
TSH IU/mL	0.005 [0.002–1.01]	1.19 [0.02–75]	<0.01
fT_3 pmol/L	12.33±5.80	3.44±0.95	<0.01
fT_4 pmol/L	17.38 [10.58–73.49]	11.33 [3.43–21.20]	<0.01
Total vertebrae T score	(-) 1.15 [(-)2.5–2.5]	(-) 0.85 [(-)2.5–2.5]	=0.03
Total vertebrae Z score	0.33 ±1.33	0.04±1.28	<0.01
Total Vertebrae BMD (g/cm^2)	0.99 [0.64–1.43]	1.03 [0.77–1.43]	<0.01
Total femur T score	(-) 1.30 [(-)2.5–1.0]	(-) 1.0 [(-)2.5–1.4]	<0.01
Total femur Z score	0 [(-)2.1–1.5]	0.30 [(-)1–1.8]	<0.01
Femur BMD (g/cm^2)	0.83 [0.56–1.09]	0.87 [0.59–1.13]	<0.01

TSH; Thyroid-stimulating hormone; fT_3: Free triiodothyronine; fT_4: free thyroxine; BMD: Bone mineral density; RAI: Radioactive iodine.

Table 2. Thyroid function tests before and after radioactive iodine treatment.

Before RAI	Female	Male	p
TSH IU/mL	0.005 (0.004–1.01)	0.005 (0.002–0.015)	NS
fT_3 pmol/L	11.31±5.32	14.42±6.37	NS
fT_4 pmol/L	19.13 (11.45–73.49)	15.69 (10.58–41.93)	NS
After RAI	**Female**	**Male**	**P**
TSH IU/mL	1.22 (0.05–35.4)	1.03 (0.02–75)	NS
fT_3 pmol/L	3.42 ±0.94	3.48±1	NS
fT_4 pmol/L	11.32 (3.43–21.20)	11.40 (10.25–18.79)	NS

TSH; Thyroid-stimulating hormone; fT_3: Free triiodothyronine; fT_4: free thyroxine; RAI: Radioactive iodine; NS: Nonsignificant.

Table 3. Total vertebrae bone mineral density and total femur bone mineral density values before radioactive iodine treatment.

Before RAI	Female	Male	p
Total vertebrae T score	(-) 1.40 [(-)2.5–2.5]	(-) 0.60 [(-)2.5–1.5]	NS
Total vertebrae Z score	(-) 0.29±1.37	(-) 0.41±1.26	NS
Total vertebrae BMD (g/cm^2)	0.96 [0.64–1.43]	1.08 [0.86–1.34]	NS
Total femur T score	(-) 1.20 [(-)2.5–1.00]	(-) 1.80 [(-)2.5– (-)0.5]	NS
Total femur Z score	0.30 [(-)2.10–1.50]	(-) 0.34 ±0.70	NS
Total femur BMD (g/cm2)	0.83 [0.56–1.09]	0.84 (0.69–1.01)	NS

BMD: Bone mineral density; RAI: Radioactive iodine; NS: Nonsignificant.

Table 4. Total comparative vertebrae BMD and femur BMD values after RAI treatment.

After RAI	Female	Male	p
Total vertebrae T score	(-) 1.80 [(-)2.5–2.5]	(-) 0.1 [(-)2.3–1.8]	NS
Total vertebrae Z score	(-)0.05±1.29	(-)0.04 ±1.29	NS
Total vertebrae BMD (g/cm^2)	0.97 [0.76–1.43]	1.16 [0.89–1.37]	NS
Total femur T score	(-) 0.90 [(-)2.5–1.4]	(-) 1.30 [(-)2.4– 0.10]	NS
Total femur Z score	0.40 [(-)1–1.8]	(-) 0.4 [(-)1–0.9]	NS
Total femur BMD (g/cm^2)	0.86 [0.59–1.13]	0.93 [0.73–1.09]	NS

BMD: Bone mineral density; NS: Nonsignificant.

DISCUSSION AND CONCLUSION

In this study, we evaluated the effects of RAI treatment on BMD by DEXA in hyperthyroid patients. The most common causes of hyperthyroidism are GD, TMNG, and TA.[6] Of the patients included in our study, 3 (7%) were GD, 24 (52%) were TA, 19 (41%) were TMNG. Note that there were more cases with nodular goiter in our study. We think that this is related to iodine deficiency in our region.

Hyperthyroidism affects many systems in the body. One of the systems that it seriously affects is bone structures. Patients with hyperthyroidism have increased bone turnover and are at risk for osteoporosis. Increased bone turnover causes bone formation and destruction. Normalization of thyroid function is associated with a decrease in bone turnover following an increase in BMD. This condition is caused by the direct effect of thyroid hormones on bone cells.[7] In addition to histological changes in the bone cortex, it has been shown that levels of osteocalcin, alkaline phosphatase, bone specific alkaline phosphatase, urinary collagen pyridinoline, which are biochemical parameters of bone resorption increased, blood calcium levels were increased, and parathyroid hormone (PTH) was suppressed. Moreover, suppressed serum PTH and increased calcium levels had returned to normal levels after the twelfth week of antithyroid treatment.[8] Biochemical parameters that show the bone metabolism of the patients were not evaluated in our study. However, the clinical complaints of the patients about bone metabolism improved in parallel with the improvement in thyroid hormone levels.

Von Recklinghausen first described hyperthyroidism as an important risk factor for low BMD in 1891. Many studies address this issue from different aspects afterward.[9,10]

BMD of women with hyperthyroidism in the reproductive period was compared with healthy (non-hyperthyroid) women in the reproductive period after 1-year follow-up; a significant decrease in BMD was found in women with hyperthyroidism compared to the control group.[11]

In postmenopausal women with hyperthyroidism, bone turnover increases and BMD decreases due to this increase. It has been shown that BMD increases when hyperthyroidism is treated.[12]

Patients with hyperthyroidism have increased bone turnover, negative calcium and phosphorus balance, and moderate osteopenia.[13] In studies with hyperthyroid patients showing improvement in the negative mineral balance following antithyroid therapy, a decrease was reported in thyroid function tests and bone mobilization parameters during the first week of treatment, but no significant change was reported in BMD. However, at the end of 1 year, it was found that the patients were euthyroid, bone and urine calcium, phosphorus, alkaline phosphatase values improved, and BMD increased.[13,14] In parallel with this study, it is worth noting that BMD partially improved in our patients at the end of the 1 year.

In another study in which biochemical parameters were studied; in untreated elderly male patients with GD, it has been shown that, while fT_4, TSH receptor antibodies, and urinary N-terminal-telopeptide levels increase, BMD of the lumbar vertebrae and femur decreases more than in women.[15] Two of our three patients with GD were found to have lower BMD than normal levels.

Treatment of hyperthyroidism should be directly correlated with the cause of the disease. For this purpose, pharmacological treatment, surgical treatment, and radioactive iodine therapy are applied. Pharmacological treatment is not widely accepted because of patient compliance, the long duration of treatment, and the recurrence of the disease with discontinuation of drugs. Although surgical treatment is a widely accepted treatment option, it has serious complications such as recurrent laryngeal nerve injury and permanent hypocalcemia.[16]

Some studies measure BMD in patients who underwent surgical treatment. In one of these studies, patients who underwent subtotal thyroidectomy because of GD in the premenopausal period were followed for three years. BMD values of patients in remission and thyrotoxicosis and healthy premenopausal women were compared. Mean lumbar and femoral BMD values were found to be significantly lower in the group with thyrotoxicosis compared to the control group and significantly higher in the remission group compared to the control group.[17]

Majima et al. demonstrated a negative correlation between TSH receptor antibodies and BMD in their study on GD. In our study, TSH levels of the patients were evaluated, but TSH receptor antibodies were not examined.[15] In our patient group, it was found to be an improvement in BMD levels except for the total vertebrae Z score while TSH levels came to normal levels. In another study by Majima et al., they divided male patients diagnosed with GD with osteopenia and osteoporosis into two groups receiving antithyroid and risedronate (antiresorptive bisphosphonate) treatment and only receiving antithyroid treatment. At the end of one year, BMD values of the lumbar spine and distal radius were measured, and significant improvement was found in BMD in the first group.[18]

Horst-Sikorska et al. showed that there was a negative correlation between low BMD and some of the gene (BsmI, ApaI, TaqI, FokI) polymorphism in young women with GD in their study.[19] We didn't work on the gene.

Studies are showing the relationship between subclinical hyperthyroidism and BMD. Lee et al. investigated the relationship between subclinical thyroid dysfunction and BMD in their study. They compared subclinical hyperthyroidism and euthyroid patients and found a significant decrease in femur BMD, whereas lumbar vertebrae BMD was not different.[20] Belaya et al. reported that subclinical hyperthyroidism due to endogenous reasons decreased BMD in postmenopausal patients with subclinical hyperthyroidism, but exogenous subclinical hyperthyroidism had no effect on BMD.[21] Another remarkable issue in the literature is the studies investigating the effect of thyroxine given in suppressive doses on BMD. In the study by Baldini et al., the effects of thyroxine treatment with suppression dose on BMD were investigated in patients with benign nodular goiter. Patients who received and did not receive thyroxine treatment were compared. There was no significant change in BMD between these two groups. They concluded that there is no significant change in BMD as thyroxine treatment slightly suppresses TSH.[22] However, the main purpose of our study is to ensure the normalization of TSH levels.

In some studies; in patients who received antithyroid medication for hyperthyroidism, Safi et al. and Ock et al. found that BMD decreased in patients with active hyperthyroidism and partial improvement was achieved when euthyroidism was achieved with treatment.[14,23] Obermayer et al. followed patients with hyperthyroidism in the postmenopausal period after RAI treatment for two years in terms of BMD. They reported that initially very low BMD values increased by 6.5% at the end of two years, but initially normal BMD values decreased by 4.3%. At the end of the study, it was thought that there may be individual differences in bone loss due to increased bone turnover and BMD after RAI treatment in patients with postmenopausal hyperthyroidism.[24] Faber et al. evaluated BMD 2 years after RAI treatment in their study on postmenopausal women with nodular goiter and subclinical hyperthyroidism. At the end of two years, they found an increase in femur BMD and vertebrae BMD and concluded that when serum TSH values return to normal levels with RAI treatment, bone loss can be prevented at least for two years.[25] When the BMD values of the patients in our study before and after the RAI treatment were compared; we found that total vertebrae T-score [(-) 1.15 → (-) 0.85], vertebrae BMD (g/cm^2) [0.99 → 1.03], total femur T-score [(-) 1.30 → (-) 1.0], total femur Z score [0 → 0.30], femur BMD (g/cm^2) [0.83 → 0.87] values increased and total vertebrae Z score [0.33 → 0.04] decreased. These changes were statistically significant ($p < 0.05$).

In the few studies with RAI treatment, for instance, the study by Aziz et al. it is reported that short-term results of RAI treatment achieved equal success with antithyroid treatment, but hypothyroidism may develop due to RAI treatment in the long term; therefore, long-term follow-up of patients is required. It is claimed that there is no significant difference between antithyroid therapy and RAI treatment in terms of its effects on BMD.[26]

Pia Nicolaisen et al. compared to a healthy control group, hyperthyroid women had lower volumetric BMD, lower estimated bone strength, and compromised cortical microarchitecture in the radius with high resolution peripheral quantitative computed tomography. After the restoration of euthyroidism, they found significant improvements in volumetric BMD and cortical microarchitecture.[27]

Dragos Apostu et al. have investigated clinical trials and meta-analyses from 2002 until 2020. And concluded thyroid disorders had an important impact on bone metabolism and fracture risk, such that hyperthyroidism, hypothyroidism, and subclinical hyperthyroidism were associated with a decreased BMD and increased risk of fracture. On the other hand, they also found subclinical hypothyroidism, was not associated with osteoporosis or fragility fractures, and subclinical hyperthyroidism treatment with RAI could improve bone health.[28]

Pedro Weslley Rosario, in a study in which he studied 36 patients one year after RAI therapy to evaluate ^{131}I therapy in elderly patients with subclinical hyperthyroidism due to nodular disease, the patients in whom TSH returned to normal, femoral and lumbar spine BMD increased by 1.9% and 1.6%, respectively, in average and found that resolution of subclinical hyperthyroidism has beneficial effects on BMD in postmenopausal women with osteopenia.[29]

Kansara et al. evaluated the effect of the antithyroid drug and RAI treatment on bone mineral content using DEXA and body composition using the bioimpedance method in hyperthyroid patients. They found bone mineral content at lumbar spine and femoral neck improved with both the therapies similarly at the end of 1 year. The body weight, protein, and fat content also increased after 1 year of observation similar between the two groups. None of the observed parameters showed a difference about the mode of the antithyroid drug.[30]

However, it is known that the frequency of side effects in patients receiving antithyroid therapy, compliance problems may occur, and close follow-up is required. For these reasons, it should be remembered that treatment may fail. As a result, there is no problem of compliance with the treatment in patients who receive RAI treatment, and their follow-up is done at longer intervals.

The improvement in clinical conditions of the patients in our study and the positive changes in BMD, except for the total vertebrae Z score, are consistent with the literature.

The strengths of our study include robust follow-up at a single center. However, our study has certain limitations, including a small sample size and a limited follow-up period of 1 year. Further long-term studies are needed to confirm the observed findings and prospective and more comprehensive studies are needed to make a clearer decision.

In conclusion, radioactive iodine therapy can be applied successfully in selected patients with hyperthyroidism. The decrease in BMD during hyperthyroidism improves after RAI treatment. The results are consistent with the current literature.

Ethics Committee Approval: This study was designed by the Declaration of Helsinki Principles and the study was approved by Sakarya University Faculty of Medicine Ethics Committee (Date: 03.01.2022, decision no: 560).

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – HTI; Supervision – HTI; Materials – HTI; Data Collection and/or Processing – HTI; Analysis and/ or Interpretation – HTI; Writing – HTI.

Peer-review: Externally peer-reviewed.

Other Information: This article was produced from my specialization thesis entitled “Evaluation of bone mineral density by densitometry in hyperthyroid patients treated with radioactive iodine-2009”

REFERENCES

1. Braverman LE UR. Introduction to thyrotoxicosis. In: Braverman LE, Utiger RD (Eds) Werner and Ingbar’s the Thyroid. 7th ed. Philadelphia: Lippincott –Raven Publisher; 1996:522-524.
2. Rivkees SA, Sklar C, Freemark M. The Management of Graves’ Disease in Children, with Special Emphasis on Radioiodine Treatment. The Journal of Clinical Endocrinology & Metabolism. 1998;83(11):3767-3776.
3. Tavintharan S, Sundram F, Chew L. Radioiodine (I-131) therapy and the incidence of hypothyroidism. Annals of the Academy of Medicine, Singapore. 1997;26(1):128-131.
4. Huysmans D, Hermus A, Corstens F, Kloppenborg P. Long-term results of two schedules of radioiodine treatment for toxic multinodular goitre. Eur J Nucl Med. 1993;20(11):1056-1062.
5. Biberoğlu S. Sekonder Osteoporoz. Editör: Gökçe Kutsal Y O, Güneş Kitabevi, Ankara; 2005:61-80.
6. Łacka K, Fraczek MM. Podział i etiopatogeneza nadczynności tarczycy [Classification and etiology of hyperthyroidism]. Pol Merkur Lekarski. 2014;36(213):206-211.
7. Delitala AP, Scuteri A, Doria C. Thyroid Hormone Diseases and Osteoporosis. J Clin Med. 2020;9(4):1034. doi:10.3390/jcm9041034
8. Seibel MJ. Biochemical markers of bone turnover: part I: Biochemistry and variability. Clin Biochem Rev. 2005;26(4):97-122.
9. Von Recklinghausen F. Die fibröse und deformierende Ostitis dOudOC, in ihren gegenseitigen Beziehungen. In: Festschrift für Rudolf Virchow. Berlin: Georg Reimer; 1891:1-89.
10. Vestergaard, P., & Mosekilde, L. Hyperthyroidism, bone mineral, and fracture risk—a meta-analysis. Thyroid. 2003;13(6), 585-593. doi:10.1089/105072503322238854
11. Ilić J, Kovacev B, Todorović-Dilas L. [Effects of hyperthyroidism on bone mass in women of reproductive age]. Med Pregl. 2004;57(3-4):111-115.
12. Guo CY, Weetman AP, Eastell R. Longitudinal changes of bone mineral density and bone turnover in postmenopausal women on thyroxine. Clin Endocrinol (Oxf). 1997;46(3):301-307.
13. Mosekilde L, Eriksen EF, Charles P. Effects of thyroid hormones on bone and mineral metabolism. Endocrinol Metab Clin North Am. 1990;19(1):35-63.
14. Safi S, Hassikou H, Hadri L, Sbihi A, Kadiri A. [Evaluation of bone mineral density in hyperthyroid patients before and after medical therapy]. Annales D'endocrinologie. 2006;67(1):27-31.
15. Majima T, Komatsu Y, Doi K, et al. Negative correlation between bone mineral density and TSH receptor antibodies in male patients with untreated Graves' disease. Osteoporosis International. 2006. doi:10.1007/s00198-006-0091-4
16. Doubleday AR, Sippel RS. Hyperthyroidism.

Gland surgery. Feb 2020;9(1):124-135.
17. Arata N, Momotani N, Maruyama H, et al. Bone mineral density after surgical treatment for Graves' disease. Thyroid. 1997;7(4):547-554.
18. Majima T, Komatsu Y, Doi K, et al. Clinical significance of risedronate for osteoporosis in the initial treatment of male patients with Graves' disease. J Bone Miner Metab. 2006;24(2):105-113.
19. Horst-Sikorska W, Ignaszak-Szczepaniak M, Marcinkowska M, Kaczmarek M, Stajgis M, Slomski R. Association analysis of vitamin D receptor gene polymorphisms with bone mineral density in young women with Graves' disease. Acta Biochim Pol. 2008;55(2):371-380.
20. Lee WY, Oh KW, Rhee EJ, et al. Relationship between subclinical thyroid dysfunction and femoral neck bone mineral density in women. Arch Med Res. 2006;37(4):511-516.
21. Belaya ZE, Melnichenko GA, Rozhinskaya LY, et al. Subclinical hyperthyroidism of variable etiology and its influence on bone in postmenopausal women. Hormones (Athens, Greece). 2007;6(1):62-70.
22. Baldini M, Gallazzi M, Orsatti A, Fossati S, Leonardi P, Cantalamessa L. Treatment of benign nodular goitre with mildly suppressive doses of L -thyroxine: effects on bone mineral density and on nodule size. Journal of Internal Medicine. 2002;251(5):407-414.
23. Ock SY, Chung YS, Choi YJ. Changes in bone mineral density and trabecular bone score in Graves' disease patients after anti-thyroid therapy. Osteoporosis and Sarcopenia. 2016;2(3):175-179.
24. Obermayer-Pietsch B, Dobnig H, Warnkross H, et al. Variable bone mass recovery in hyperthyroid bone disease after radioiodine therapy in postmenopausal patients. Maturitas. 2000;35 (2):159-166.
25. Faber J, Jensen IW, Petersen L, Nygaard B, Hegedüs L, Siersbaek-Nielsen K. Normalization of serum thyrotrophin by means of radioiodine treatment in subclinical hyperthyroidism: effect on bone loss in postmenopausal women. Clinical Endocrinology. 1998;48(3):285-290.
26. Azizi F, Abdi H, Cheraghi L, Amouzegar A. Treatment of subclinical hyperthyroidism in the elderly: Comparison of radioiodine and long-term methimazole treatment. Thyroid. 2021;31(4):545-551.
27. Nicolaisen P, Obling ML, Winther KH, et al. Consequences of hyperthyroidism and its treatment for bone microarchitecture assessed by high -resolution peripheral quantitative computed tomography. Thyroid. 2021;31(2):208-216.
28. Apostu D, Lucaciu O, Oltean-Dan D, et al. The Influence of Thyroid Pathology on Osteoporosis and Fracture Risk: A Review. Diagnostics (Basel, Switzerland). 2020;10(3):149. doi:10.3390/ diagnostics10030149
29. Rosario PW. Radioiodine therapy in elderly patients with subclinical hyperthyroidism due to nonvoluminous nodular goiter and its effect on bone metabolism. Arq Bras Endocrinol Metabol. 2013;57(2):144-147.
30. Kansara S, Kotwal N, Kumar KVSH, Singh Y, Upreti V, Nachankar A. Effect of antithyroid therapies on bone and body composition: A prospective, randomized, clinical study comparing antithyroid drugs with radioiodine therapy. Indian J Endocrinol Metab. 2017;21(4):531 -534. doi: 10.4103/ijem.IJEM_103_17